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Title: Transport container for keeping frozen material chilled

Description:

The invention relates to a transport container for keeping frozen material chilled, in particular frozen biological tissue samples or cell cultures, with an insulation which encloses an insulating chamber, with an inner container which is removably arranged in the insulating chamber and receives the frozen material in a chamber, and with a refrigerant which gives off cold by phase transformation.

A long-known measure for keeping material chilled is to put the material in an insulating container and in this way protect it from exposure to heat. In particular in the case of a transport container, however, there are limits to the wall thickness of the insulation, and consequently the insulating effect. Therefore, in particular in the case of relatively long storage or transporting times, there is no alternative but to ensure that penetrating heat is compensated by corresponding production of cold, in order to avoid a damaging rise in the temperature or even thawing of frozen material.

It is known to provide the cold that is required to compensate for heat flowing in by means of a refrigerant at low temperature, which is introduced in addition with the material into the correspondingly overdimensioned insulating chamber of the transport container. In this case, there is no need for the expense of a chilling device with media that has to be circulated. Exploiting the phase transformation of the refrigerant in the solid → liquid transition (heat of melting), liquid → gaseous transition (heat of evaporation) or solid → gaseous transition (heat of

sublimation) allows a constant temperature to be achieved for the duration of the transformation, which depends on the quantity involved.

Known examples of such refrigerants used in transport containers are ice (water), dry ice (carbon dioxide) and liquid nitrogen. While ice has too high a melting point, of 0°C, to be used for keeping frozen material chilled, the temperature of sublimation of solidified carbon dioxide and the temperature of ebullition of liquid nitrogen are significantly below the customary temperatures of frozen material, so that to avoid excessive chilling of the frozen material additional measures, such as an insulating wall between the refrigerant and the material, have to be taken to provide correct temperature control. In particular, however, there is also the fact that here the transformation respectively takes place into the gaseous phase, so that comparatively large volumes of gas occur and have to be discharged to the outside. In confined spaces, this leads to problems, which for example makes it more difficult for a corresponding transport container to be transported in an aircraft.

The invention is based on the object of providing a comparatively small and lightweight, and consequently handy, transport container with which the frozen material is reliably kept at the intended chilling temperature in a simple way during a predetermined transporting period, without gases thereby being released and without measures for preventing excessive chilling of the material being required.

This object is achieved according to the invention by providing at least one chilling chamber for the material and at least one refrigerant chamber which is separate from the chilling chamber, contains the

refrigerant and is permanently hermetically sealed, by providing a refrigerant with a solid/liquid phase transition in the temperature range from -15° to -100°C and by the insulation being a superinsulation with a coefficient of thermal conductivity λ of ≤ 0.01 W/m K.

Mercury or organic substances or mixtures for which the phase transformation temperature preferably lies between -30° and -85°C come into consideration as refrigerants. Solidified mercury has a melting point of about -39°C (at atmospheric pressure). This temperature is very suitable for keeping biological material chilled, such as tissue samples or cell cultures that are for example being sent for the analysis of proteins and RNA to diagnose medical conditions (cancer) and precludes damage caused by excessive chilling. A further advantage is that, when the refrigerant is used, neither gas nor vapor occurs and there is virtually no change in volume during the phase transformation.

In the case of the transport container according to the invention, the refrigerant remains inaccessible in the housing of the refrigerant chamber or in the inner container. The mercury that has liquefied (been used) after transport can be reconditioned by means of a phase transformation back from liquid → solid for a new refrigerated transporting operation, by freezing the removable refrigerant container or inner container, for example by immersion in liquid nitrogen.

Expedient refinements and developments of the transport container according to the invention are provided by the subclaims. These are also directed at particularly simple production and handling of the transport container and at adaptation of the chilling capacity to

the transporting distance to be covered, and consequently the chilling period.

Exemplary embodiments of the transport container according to the invention are explained in more detail below on the basis of a schematic drawing, in which:

Figure 1 shows the transport container with significant parts in vertical section;

Figure 2 shows the transport container in a horizontal cross section along line II-II;

Figure 3 shows the inner container from Figure 1 in vertical section and on an enlarged scale;

Figure 4 shows one of the two additional containers from Figure 1 - likewise in vertical section and on an enlarged scale;

Figure 5 shows an insulating stopper intended to be exchanged for an additional container, and having corresponding dimensions, in side view;

Figure 6 shows a modified inner container in a representation corresponding to Figure 3;

Figure 7 shows a section along line VII-VII in Figure 6;

Figure 8 shows an enlargement of a detail with the closed filling opening from Figure 6;

Figure 9 shows an additional container modified as compared with Figure 4;

Figure 10 shows an inner container similar in its configuration to Figures 3 and 6;

Figure 11 shows a horizontal section along line XI-XI in Figure 10;

Figure 12 shows an additional container similar in its configuration to Figures 4 and 9;

Figure 13 shows a ground stopper in a representation comparable to Figure 8;

Figure 14 shows the stopper according to Figure 13 after applying a coating;

Figure 15 shows the stopper fitted into the filling opening, with external welding;

Figure 16 shows the arrangement according to Figure 15 after finishing;

Figure 17 shows the stopper fitted into the filling opening without welding;

Figure 18 shows the arrangement according to Figure 17 after a finishing operation; and

Figure 19 shows an inner container with additional jacket chilling by means of a refrigerant melting at a higher temperature in axial section.

The transport container 1 according to Figures 1 and 2 is cylindrically formed. It comprises in coaxial arrangement a likewise cylindrical inner container 2 and two likewise cylindrical additional containers 3, 4, which are arranged at the ends above and below the

inner container 2 in an insulating chamber 5. The insulating chamber 5 is formed by a thick-walled cup-shaped insulation 6 with an inwardly stepped upper edge 7, which receives a correspondingly stepped thick-walled insulating closure 8 in the form of a cover, which closes the insulating chamber 5. The insulation 6 is closely enclosed by a rigid protective tube 9, which is respectively provided at both its ends with an external thread, firmly screwed with which is the engaging-over threaded edge 10 of a screw cover 11 and 12, respectively.

The insulation 6 and the insulating closure 8 consist of a high-grade thermal insulating material with a very low coefficient of thermal conductivity λ of, for example, 0.002 W/m K. This known thermal insulating material is also referred to as superinsulation because of the outstanding insulating effect.

The inner container 2 is represented in Figure 3. It comprises a hollow housing or cup part 13 and a screw cover 14 which can be screwed with it. Formed in the cup part 13 are a likewise cup-shaped refrigerant chamber 15 and a central chilling chamber 16, which is closed by means of the screw cover 14. The chilling chamber 16 receives the material 17 that is to be kept chilled and transported, in the case represented a sample in a sample container 18, the upper end of which is closed by a closure part 19. The refrigerant chamber 15 is filled with a refrigerant 15' (for example mercury), which is represented refrigerated in the solid state. To allow the refrigerant 15' to be introduced, the cup part 13 is centrally provided at its bottom with a filling opening 20, which has a thread into which a hexagon socket screw stopper 21 is screwed. The screw stopper 21 is dimensioned in such a way and screwed into the filling opening 20 to such an

extent that there is an outer bottom depression 22 on the cup part 13. This bottom depression 22 receives a welding bead 23, which is created when the filling opening 20 is welded closed. Accordingly, the refrigerant chamber 15 is permanently hermetically sealed, so that there need be no fear of refrigerant 15' escaping.

The cup part 13 and the screw cover 14 are produced from a high-strength material, in order that compressive and shock loads can be absorbed without deformation, and it can be ensured that no damage or escape of refrigerant (mercury) occurs even in extreme situations such as an aircraft crash. Suitable materials for the inner container 2 are, for example, high-grade steel, titanium or titanium alloys (TiAl5Sn2), which not only have high strength but are also comparatively light, which reduces the transport weight. In the case of refrigerants that are less toxic than mercury, other materials such as aluminum or low-temperature resistant plastic also come into consideration.

According to Figure 4, the additional containers 3 and 4 are likewise hollow-cylindrically formed with a refrigerant chamber 24, but without a chilling chamber. The refrigerant chamber 24 is likewise filled with a refrigerant 24', and as in Figure 3 the additional containers 3, 4 are respectively provided centrally at the bottom with a filling opening 25, a screw stopper 26 and a welding bead 27. The additional containers 3, 4 may likewise be produced from the aforementioned materials.

Figure 5 shows a cylindrical insulating stopper 28 in the dimensions of the additional containers 3, 4. Such insulating stoppers 28 may be inserted in the chilling

chamber 16 in place of the additional containers 3, 4 if, in the case of a correspondingly short transporting distance or transporting period, the refrigerant 15' in the inner container 2 is definitely already sufficient to keep the material 17 chilled during transport.

According to Figure 6, an inner container 30 which can be used in place of the inner container 2 is provided. The inner container 30 is cylindrically shaped and has a central cylindrical chilling chamber 31, which extends from its upper side and is enclosed by an annular refrigerant chamber 32 with the spacing of the wall. This refrigerant chamber 32 ends with the spacing of the wall from the upper end face and the lower end face of the inner container 30. Here, too, the refrigerant chamber 32 is filled with refrigerant 32'. To introduce it, a filling opening 33 that slightly tapers conically toward the refrigerant chamber 32 is formed in the upper end face of the inner container 30, as Figure 8 shows in particular. After introducing the refrigerant 32', the filling opening 33 was closed by means of a stopper 34, which may likewise consist of high-grade steel or titanium. Above the stopper 34, the filling opening 33 is welded closed by means of a welding bead 35.

The conical stopper 34 may be appropriately fitted with a press fit, in that it is shrunk before fitting by intense supercooling. An annular seal 36 of amalgam-forming metal, such as for example copper, may also be optionally fitted at the same time. This is accompanied by formation of an amalgam (Hg-Cu alloy), and it may be possible to dispense with welding closure by means of the welding bead 37.

Figure 9 shows an additional container 37, which may likewise be produced from high-grade steel or titanium.

This additional container 37 also has a a refrigerant chamber 38 filled with refrigerant 38', a formation corresponding to Figure 4 or Figure 8 being provided for the filling and closing operation (not represented in Figure 9).

The additional container 37 has on its upper end face a central, short threaded stub 39, which fits into a central, internally threaded bore 40 on the underside of the inner container 30. Therefore, the additional container 37 can be firmly connected to the inner container 30 and close contact between the containers 30 and 37 can be thereby achieved, which ensures a good heat transfer.

A further additional container 37 can be connected to the inner container 30 in a corresponding way at the top. The internal thread 41 on the upper edge of the chilling chamber 31 serves for this purpose. This is given such an axial length that a screw stopper 42 for closing the chilling chamber 31 can be screwed in by means of a hexagon socket wrench to such an extent that the threaded stub 39 of the additional container 37 can also be screwed into the upper end of the internal thread 40.

Figure 10 shows another inner container 44, which comprises a cylindrical block 45 of high-grade steel or titanium, in which a multiplicity of bores are machined, extending from the upper end face. To be specific, according to Figure 11, a central bore is provided along the cylindrical axis and is surrounded by an inner ring of coaxial bores, which is enclosed by an outer ring of coaxial bores. The central bore and the bores of the inner ring form chilling chambers 46, so that altogether seven sample containers 18 according to Figure 3 can be received. The twelve bores of the

outer ring form refrigerant chambers 47, which in each case have a refrigerant filling 47'. At their upper end, the refrigerant chambers 47 are closed by means of a stopper 48, which may be screwed in or inserted by means of heat shrinkage and held with a press fit.

An additional safeguard against escape of refrigerant 47' is achieved by providing a cover ring 49, which covers over the outer ring of refrigerant chambers 46 and is firmly welded to the cylinder block 45, as Figure 10 shows.

The cover ring 49 has an internal thread 50, in which a disk-shaped screw stopper 51 is screwed with its external thread 52, terminating flush with the cover ring 49 on the top side. The screw stopper 51, which terminates the chilling chambers 46, has on its upper side two pairs of diametrically opposed bore holes 53, offset by 90° in relation to one another, for placing a pin wrench when screwing in or unscrewing. The cover ring 49 has two diametrically opposed grooves 54, which form two parallel flats for placing a wrench, in order that a high screwing force can be applied to the screw stopper 51.

According to Figure 12, an additional container 55 in the form of a cylinder block 56 is also provided, having in a way similar to the cylinder block 45 an outer ring and an inner ring of bores, but no central bore. Here, both rings of bores form refrigerant chambers 57, which receive a refrigerant filling 57'. The refrigerant chambers 57 are respectively closed at their upper ends by means of a stopper 58, which like the stopper 48 in Figure 10 may be screwed in or fitted by means of cold shrinkage with a press fit.

The cylinder block 56 is provided at the top with a central threaded stud 59 for connection to the inner container 44 according to Figure 10. Accordingly, the cylinder block 45 has at the bottom a central threaded bore 60. A corresponding threaded bore 61 is provided centrally on the upper side of the screw stopper 51, so that an additional container 55 according to Figure 12 can be connected to both ends of the inner container 44.

Figure 13 shows in an enlarged representation corresponding to Figure 8 a different, conical stopper 62 for closing the conical filling opening 33, but still before insertion. The stopper 62 has a shank-shaped attachment 63, which serves the purpose of rotating the conical stopper 62 and grinding it into the filling opening 33. After this fitting-in of the stopper 62, it is provided with an electrolytic coating 64 of amalgam-forming metal, as Figure 14 shows.

The stopper 62 with the coating 64 is then fitted into the filling opening 33, expediently by means of heat shrinkage, so that it is held in the filling opening 33 with a press fit. With preference, two fitting variants come into consideration for this: according to Figure 15, the stopper 62 is arranged in the filling opening 33 in a countersunk manner, corresponding to the dimensions chosen, whereupon supplementary welding-closure takes place by means of the welding bead 65. In a finishing step, the stopper 62 and the protruding welding bead 65 are then provided with a smooth machining surface 66, which terminates flush with the surface 68 of the housing or inner container 30 having the refrigerant chamber 32, as Figure 16 shows.

By the alternative according to Figure 17, the stopper 62 completely fills the filling opening 33. Here, the

protruding part of the stopper 62, and in particular the entire shank-shaped attachment 63, are removed as far as a machining surface 67, which according to Figure 18 terminates flush with the surface 68 of the housing or inner container 30 receiving the refrigerant chamber 32.

The inner container 70 according to Figure 19 corresponds largely to the inner container 2 represented in Figure 3. The cylindrical U-shaped inner container 70 has a refrigerant chamber 71, which is filled with the refrigerant 71'. An inner wall 72 and an outer wall 73 delimit the refrigerant chamber 71, which has been filled with refrigerant 71' and hermetically sealed in the way already described above, which is not represented in Figure 19. The inner wall 72 encloses a chilling chamber 74, which is intended for receiving the sample. An inner insulation 75, once again configured as superinsulation, encloses the refrigerant chamber 71. This inner insulation 75 is enclosed by a substantially cylindrical wall 76. The upper end of the chilling chamber 74 is once again closed by a cover 77, which is not represented in section and comprises a stopper screwed into the upper end of the inner wall 72 and a cover plate with an insulating effect. The inner container 70 could be used already in the configuration described thus far if an increased refrigerating capacity is not required because of a short transporting period and storage time.

The special feature of the inner container 70 is that it has a jacket chamber 78, which encloses the wall 76 and contains a refrigerant 78' melting at a higher temperature in comparison with the refrigerant 71', with a melting point in the range from 0° to -15°C, and is enclosed by a jacket wall 79. An insulating jacket

80 with an outer container wall 81 encloses the jacket chamber 78. The insulating jacket 80, once again configured as superinsulation, is formed in two parts with a cup-shaped bottom jacket part 82 and a conversely cup-shaped cover jacket part 83, so that the cover jacket part 83 can be removed in order to make the cover 77, and consequently the chilling chamber 74, accessible. In the position for use (shipping position) shown in Figure 19, the bottom jacket part 82 and the cover jacket part 83 lie with their end faces against each other. In this case, in the region of the parting plane, a narrow inner stepped ring 84 is provided on the bottom jacket part 82 and a narrow outer stepped ring 85 is provided on the top jacket part 2 and engages over the inner stepped ring 84. As a result, increased penetration of heat in the region of the parting plane is prevented.

The use of two different refrigerants 71' and 78', envisaged according to Figure 19, has the advantage that the required amount of refrigerant 71', which is generally more or less toxic and therefore critical, can be reduced, and a less toxic or even non-toxic refrigerant (for example water or brine), which melt/solidifies at a slightly higher temperature in the range from 0 to 15°C, can be used instead.

The transport container 1 is used for example to transport one or more frozen tissue samples from one location to another location at which there are respectively stationary chilling devices for freezing. The shipping operation is therefore an intermediate link in a chilling chain. The shipping may be performed for example by means of courier services, which ensure transportation even to remote locations of the world within a comparatively short time of 1, 2 or

3 days. To be specific, the following procedure is followed here:

The sender first provides freezing of the inner container 2, 30, 44, 70 and the additional containers 3, 4, 37, 55 with liquid nitrogen involving complete solidification of the refrigerant filling 15', 24', 32', 38', 47', 57', 71', 78'. Then, the sample 17 placed in the sample container 18 is inserted into the chilling chamber 16, 31, 46, 74 and the latter is closed with the screw cover 14, 77 or the screw stopper 42, 51. The inner container 2, 30, 44, 70, and if appropriate the additional containers 3, 4; 37, 55, are then placed in the insulation 6, in the case of the inner container 30, 44 the additional containers 37, 55 first being firmly screwed with the inner container 30, 44 if they are required for an increased chilling capacity, for example over a long transporting distance. After that, the insulating cover 8 is placed on and the screw cover 11 is firmly screwed on, whereupon the transport container 1 is shipped with as little delay as possible.

The recipient opens the transport container 1 and removes the sample container 18 with the sample 17 in the reverse sequence. The temperature in the insulating chamber 5 of the insulation 6 or in the chilling chamber 16, 31, 46, 74, which must for example lie around -40°C to correspond to the melting point of the refrigerant, is expediently measured by the recipient when the transport container 1 is opened. If it is not at this temperature, it is established that the chilling capacity of the refrigerant filling 15', 24', 32', 38', 47', 57', 71', 78' has not been adequate because the transporting time has been grossly exceeded, so that the sample 17 may possibly have become damaged and must then be rejected.

A transport container 1 provided with a 5 cm thick superinsulation in accordance with the above specifications has, for example, an outside diameter of 24 cm and a length of 24 cm and is consequently handy and ideally suited for shipping by courier.